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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/937,756	09/25/1997	DAVID C. RUEGER	JJJ-P06-504	2132
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Erika Takeuchi				
ROPES & GRAY LLP				
45 Rockefeller Plaza				
New York, NY 10111-0087				
			EXAMINER	
			WANG, CHANG YU	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

08/937,756

Applicant(s)

RUEGER ET AL.

Examiner

Chang-Yu Wang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/30/07.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 97,99 and 105-113 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 97,99 and 105-113 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION
RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 30, 2007 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed July 30, 2007 is acknowledged. Claims 1-96 are cancelled. Claims 97, 99, 111, 113 are amended. Claims 97, 99, 105-113 are pending in this application and under examination in this office action.
3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.
4. Applicant's arguments filed on July 30, 2007 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Maintained

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 97, 99, 105-113 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of decreasing neuronal death associated with a neuropathy or injury in which neuronal survival is mediated by expression of NCAM or L1 by administering to a subject with a morphogen comprising a dimeric protein having fragments of amino acids 38-139 and 43-139 of SEQ ID NO:5 with homology as recited in claim 97, does not reasonably provide enablement for a method for decreasing neuronal cell death associated with all forms of neuropathy or injury comprising administering a morphogen to a subject afflicted with a neuropathy associated with reduced N-CAM or L1 isoform activities or all forms of chemical or physical injury as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The rejection is maintained for the reasons made of record in the office actions mailed on 11/02/06 & 5/27/07.

At p. 7 of the response, Applicant argues that amended claims are enabled because the amendment to the claims can be found throughout the specification (p.6, p.76, p.79 and p. 80) to support the effects of morphogens on neuronal survival is via production of NCAM or L1 in vitro.

In contrast to Applicant's assertion, the recitation of "a neuropathy associated with reduced NCAM or L1 isoform activities" was not clearly disclosed in the specification and claims as filed. Applicant only describes neuropathy in the specification but fails to define/describe what is encompassed within a neuropathy

associated with reduced NCAM or L1 isoform activities. A skilled artisan cannot contemplate an undefined neuropathy since it is not clear what form of neuropathy is associated with reduced NCAM or L1 isoform activities and it is also not clear what specific activities of NCAM or L1 isoforms are reduced and thus would be associated with a specific form of neuropathy.

At p. 7 of the response, Applicant argues that the specification provides a working example (Example 8) to treat damage of optic nerve, which is considered to be part of the CNS. In addition, Applicant argues that the Patent office granted US6495513, which is directed to nerve gap repair but is not limited to the PNS. Applicant's arguments have been fully considered but they are not persuasive.

In response to Applicant's argument that US6495513 is not limited to the PNS, the examiner asserts that the patentability of each application is judged by its own merits. In this case, Applicant fails to reasonably demonstrate the claimed method can be used in the claimed method since the status of the art in the CNS regeneration is unpredictable.

In contrast to Applicant's assertion, as previously made of record, neither the specification nor the prior art supports the claimed invention used in the CNS since once neurons of the CNS die they cannot be regenerated. In addition, in contrast to Applicant's assertion with regard to the working example of optic nerve in example 8, the examiner asserts Applicant is incorrect. Based on Applicant's own admission, the CNS neuronal cell death cannot be rescued. See p. 83 of the specification below

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"Following axonal damage in vivo the CNS neurons are unable to resprout processes. Accordingly, trauma to CNS nerve tissue, including the spinal cord, optic nerve and retina, severely damages or destroys the neural pathways defined by these cells. Peripheral nerve grafts have been used in an effort to bypass CNS axonal damage. Successful autologous graft repair to date apparently requires that the graft site occur near the CNS neuronal cell body, and a primary result of CNS axotomy is neuronal cell death. The efficacy of morphogens described herein on CNS nerve repair, may be evaluated using a rat crushed optic nerve model..." (p.83 of the specification).

Since the status of art in the CNS regeneration is unpredictable and Applicant has not successfully demonstrated the claimed morphogen and the claimed method can be used to reduce neuronal cell death in optic nerve damage, a description of a prophetic example is not sufficient to demonstrate the claimed method is enabled in the CNS.

Further, although the optic nerve is considered to be part of the CNS, the optic nerve does not contain neuronal cell bodies. The neuronal cell bodies of the optic nerve are located in the occipital lobes of the brain. Once cell bodies are damaged, they cannot be regenerated. The invention must be enabled at the time of filing and, therefore, the enablement cannot be supported by later obtained experimental results. In *In re*

Rasmusson the Court held that

"If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis". *In re Rasmusson v. SmithKline Beecham Corp.* 75 USPQ2D 1297, p1301.

Furthermore, while the specification teaches decreasing neuronal death caused by sciatic nerve injury or optic nerve injury by OP-1 in vitro, it does not provide sufficient guidance as to whether neuronal death could be decreased in all forms of neuropathy, including those caused by different diseases, chemical or physical injury by OP-1 or related morphogens since the causes of all forms of neuropathy or injury are very

divergent. For example, the causes of neurodegenerative diseases are not clear. It could be due to the problem of protein processing of APP Alzheimer's disease or poly-Q accumulation for Huntington's disease. However, these different diseases do not have a established correlation with the cause, the effects obtained in vitro does not correlated with the effects in vivo in different neurodegenerative diseases or different forms of neuropathy. Thus, it is unpredictable whether neuronal cell death could be decreased in all forms of neuropathy, including those caused by different disease, chemical, or physical injury by administration of OP-1 or related morphogens since the causes are divergent and unpredictable.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, it is unpredictable whether the claimed morphogen can be used to reduce neuronal cell death in all forms of neuropathy or injury, and the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation. In addition, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc. v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the

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specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement”.

The instant specification is not enabling because one can not following the guidance presented therein and practice the claimed method without first making a substantial inventive contribution. Accordingly, the rejection of claims 97, 99, 105-113 under 35 U.S.C. §112, first paragraph, because the specification does not enable the invention commensurate in scope with the claims is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 97, 99, 105-113 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims 97 and 112 as amended are directed to a method for decreasing neuronal cell death associated with a neuropathy by a morphogen. The claims 99 and 113 as amended are directed to a method for decreasing neuronal cell death associated with a chemical or physical injury by a morphogen. Claims 105-111 depend from claims 97, 99, 112 and 113. The instant claims 97 and 112 now recite limitation of “a

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neuropathy associated with reduced NCAM or L1 isoform activities", which was not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. In addition, claims 99 and 113 now recite limitation of "chemical injury is caused by lead, ethanol, ammonia, organic solvents, formaldehyde, cigarette smoke, opiates or glutamate". The limitation "a neuropathy associated with reduced NCAM or L1 isoform activities" and the limitation "lead, ammonia, organic solvents, formaldehyde" were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant fails to disclose "a neuropathy associated with reduced NCAM or L1 isoform activities" as recited in claims 97 and 112. The specification only discloses neuropathy. Applicant provides no guidance as to what is encompassed in the recitation of "a neuropathy associated with reduced NCAM or L1 isoform activities". In addition, Applicant fails to disclose "lead, ammonia, organic solvents, formaldehyde" as recited in claims 99 and 113. The specification only discloses ethanol, ammonia, cigarette smoke, opiates and glutamate. Accordingly, in the absence of sufficient recitations of "a neuropathy associated with reduced NCAM or L1 isoform activities" and "lead, ammonia, organic solvents, formaldehyde", the original specification does not provide adequate written description to support these limitations as recited in claims 97, 99, 112 and 113. Thus these recitations constitute new matter absent evidence for their support.

Applicant is required to cancel the new matter in the reply to this office action.

Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 97, 105-112 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 97, 105-112 are indefinite because claims 97 and 112 recite “a neuropathy associated with reduced NCAM or L1 isoform activities” and the rest of claims are indefinite as depending from indefinite claims 97 and 112. Applicant only describes neuropathy in the specification but fails to define/describe what is encompassed within a neuropathy associated with reduced NCAM or L1 isoform activities. The disclosure fails to set forth the metes and bounds of what is encompassed within the definition of such a neuropathy associated with reduced NCAM or L1 isoform activities and thus the claims are indefinite.

In addition, Applicant recites “activities” in the claims. Although Applicant describes several activities of NCAM or L1 on p.34, this description is not definite: there is no limitation on what would or would not be considered an “activity” and thus be within the scope of the claims.

Claim Objections

8. Claims 105-111 are objected to because they improperly depend from claims with a higher number. Appropriate correction is required.

9. Applicant is advised that should claims 97 and 99 be found allowable, claims 112 and 113 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

9. NO CLAIM IS ALLOWED.

10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are

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unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/

Chang-Yu Wang, Ph.D.

October 9, 2007

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud